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SEQUENCE LISTING

<110> MEDICO, ER  
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<120> RECOMBINANT PROTEINS DERIVED FROM HGF AND MSP

<130> 0471-0162P

<140> US 09/600,991

<141> 2000-09-15

<160> 22

<170> PatentIn version 3.1

<210> 1

<211> 1725

<212> DNA

<213> Artificial Sequence

<220>

<223> Magic F-1 DNA coding sequence

<400> 1

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cccagacaagg	gctttgatga	taattattgc	cgcaatcccc	atggccagcc	gaggccatgg	1620
tgtctatactc	ttgaccttca	caccgcgtgg	gagtactgtg	caattaaaac	atgcgctgac	1680
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40

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<210> 2  
 <211> 574  
 <212> PRT  
 <213> Artificial Sequence

<220>

<223> Magic F-1 recombinant protein obtained combining hairpin loop and  
 kringle domains of human HGF and MSP

<400> 2

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Arg	Lys	Arg	Arg	Asn	Thr	Ile	His	Glu	Phe	Lys	Lys	Ser	Ala	Lys	Thr	35	40	45	
Thr	Leu	Ile	Lys	Ile	Asp	Pro	Ala	Leu	Lys	Ile	Lys	Thr	Lys	Lys	Val	50	55	60	
Asn	Thr	Ala	Asp	Gln	Cys	Ala	Asn	Arg	Cys	Thr	Arg	Asn	Lys	Gly	Leu	65	70	75	80
Pro	Phe	Thr	Cys	Lys	Ala	Phe	Val	Phe	Asp	Lys	Ala	Arg	Lys	Gln	Cys	85	90	95	
Leu	Trp	Phe	Pro	Phe	Asn	Ser	Met	Ser	Ser	Gly	Val	Lys	Lys	Glu	Phe	100	105	110	
Gly	His	Glu	Phe	Asp	Leu	Tyr	Glu	Asn	Lys	Asp	Tyr	Ile	Arg	Asn	Cys	115	120	125	
Ile	Ile	Gly	Lys	Gly	Arg	Ser	Tyr	Lys	Gly	Thr	Val	Ser	Ile	Thr	Lys	130	135	140	
Ser	Gly	Ile	Lys	Cys	Gln	Pro	Trp	Ser	Ser	Met	Ile	Pro	His	Glu	His	145	150	155	160
Ser	Tyr	Arg	Gly	Lys	Asp	Leu	Gln	Glu	Asn	Tyr	Cys	Arg	Asn	Pro	Arg	165	170	175	
Gly	Glu	Glu	Gly	Gly	Pro	Trp	Cys	Phe	Thr	Ser	Asn	Pro	Glu	Val	Arg	180	185	190	
Tyr	Glu	Val	Cys	Asp	Ile	Pro	Gln	Cys	Ser	Glu	Val	Glu	Cys	Met	Thr	195	200	205	
Cys	Asn	Gly	Glu	Ser	Tyr	Arg	Gly	Leu	Met	Asp	His	Thr	Glu	Ser	Gly	210	215	220	
Lys	Ile	Cys	Gln	Arg	Trp	Asp	His	Gln	Thr	Pro	His	Arg	His	Lys	Phe	225	230	235	240

Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe Asp Asp Asn Tyr Cys Arg  
 245 250 255  
 Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys Tyr Thr Leu Asp Pro His  
 260 265 270  
 Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr Cys Ala Asp Lys Ala Ser  
 275 280 285  
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Leu  
 290 295 300  
 Glu Gly Gln Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser  
 305 310 315 320  
 Ala Lys Thr Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr  
 325 330 335  
 Lys Lys Val Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn  
 340 345 350  
 Lys Gly Leu Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg  
 355 360 365  
 Lys Gln Cys Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys  
 370 375 380  
 Lys Glu Phe Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile  
 385 390 395 400  
 Arg Asn Cys Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser  
 405 410 415  
 Ile Thr Lys Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro  
 420 425 430  
 His Glu His Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn Tyr Cys Arg  
 435 440 445  
 Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr Ser Asn Pro  
 450 455 460  
 Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser Glu Val Glu  
 465 470 475 480  
 Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met Asp His Thr  
 485 490 495  
 Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln Thr Pro His Arg  
 500 505 510  
 His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe Asp Asp Asn  
 515 520 525  
 Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys Tyr Thr Leu  
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Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr Cys Ala Asp  
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Lys Ala Asp Asp Asp Asp Lys His His His His His His His  
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 <211> 1692  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Metron F-1 DNA coding sequence

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 gtggtgcccg ggccttggca ggaggatgtg gcagatgctg aagagtgtgc tggtcgctgt 180  
 gggcccttaa tggactgccg ggccttccac tacaacgtga gcagccatgg ttgccaactg 240  
 ctgccatgga ctcaacactc gcccacacag aggtgcggc gttctgggcg ctgtgacctc 300  
 ttccagaaga aagactacgt acggacctgc atcatgaaca atgggggttg gtaccggggc 360  
 accatggcca cgaccgtggg tggcctgccc tgccaggctt ggagccacaa gttcccgaat 420  
 gatcacaagt acacgccac tctccggaat ggcttggga agaatctctg ccgtaaccct 480  
 gatggcgacc ccggaggtcc ttggtgctac acaacagacc ctgctgtgcg cttccagagc 540  
 tgccggcatca aatcctgccg ggaggccgcg tgtgtctggt gcaatggcga ggaataccgc 600  
 ggcgcggtag accgcacgga gtcaggggcg gagtgccagc gctgggatct tcagcaccgc 660  
 caccagcacc ccttcgagcc gggcaagtcc ctgcaccaag gtctggacga caactattgc 720  
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 aataaaggac ttccattcac ttgcaaggct tttgtttttg ataaagcaag aaaacaatgc 1080  
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 ctcatggatc atacagaatc aggcaagatt tgtcagcgct gggatcatca gacaccacac 1500  
 cggcacaat tcttgctga aagatatccc gacaagggt ttgatgataa ttattgccgc 1560  
 aatcccgatg gccagccgag gccatggtgc tatactcttg accctcacac ccgctgggag 1620  
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<210> 4  
 <211> 563  
 <212> PRT  
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 <223> Metron F-1 recombinant protein obtained combining hairpin loop and  
 kringle domains of human HGF and MSP

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			20					25					30		
Glu	Leu	Gln	His	Leu	Leu	His	Ala	Val	Val	Pro	Gly	Pro	Trp	Gln	Glu
		35					40					45			
Asp	Val	Ala	Asp	Ala	Glu	Glu	Cys	Ala	Gly	Arg	Cys	Gly	Pro	Leu	Met
	50					55					60				
Asp	Cys	Arg	Ala	Phe	His	Tyr	Asn	Val	Ser	Ser	His	Gly	Cys	Gln	Leu
65					70					75					80
Leu	Pro	Trp	Thr	Gln	His	Ser	Pro	His	Thr	Arg	Leu	Arg	Arg	Ser	Gly
				85					90					95	
Arg	Cys	Asp	Leu	Phe	Gln	Lys	Lys	Asp	Tyr	Val	Arg	Thr	Cys	Ile	Met
			100					105					110		
Asn	Asn	Gly	Val	Gly	Tyr	Arg	Gly	Thr	Met	Ala	Thr	Thr	Val	Gly	Gly
		115					120					125			
Leu	Pro	Cys	Gln	Ala	Trp	Ser	His	Lys	Phe	Pro	Asn	Asp	His	Lys	Tyr
	130					135					140				
Thr	Pro	Thr	Leu	Arg	Asn	Gly	Leu	Glu	Glu	Asn	Phe	Cys	Arg	Asn	Pro
145					150					155					160
Asp	Gly	Asp	Pro	Gly	Gly	Pro	Trp	Cys	Tyr	Thr	Thr	Asp	Pro	Ala	Val
				165					170					175	
Arg	Phe	Gln	Ser	Cys	Gly	Ile	Lys	Ser	Cys	Arg	Glu	Ala	Ala	Cys	Val
			180					185					190		
Trp	Cys	Asn	Gly	Glu	Glu	Tyr	Arg	Gly	Ala	Val	Asp	Arg	Thr	Glu	Ser
		195					200					205			
Gly	Arg	Glu	Cys	Gln	Arg	Trp	Asp	Leu	Gln	His	Pro	His	Gln	His	Pro
	210					215					220				
Phe	Glu	Pro	Gly	Lys	Phe	Leu	Asp	Gln	Gly	Leu	Asp	Asp	Asn	Tyr	Cys
225					230					235					240
Arg	Asn	Pro	Asp	Gly	Ser	Glu	Arg	Pro	Trp	Cys	Tyr	Thr	Thr	Asp	Pro
				245					250					255	
Gln	Ile	Glu	Arg	Glu	Phe	Cys	Asp	Leu	Pro	Arg	Cys	Gly	Ser	Glu	Ala
			260					265					270		
Gln	Pro	Arg	Leu	Glu	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly
		275					280					285			
Gly	Gly	Gly	Ser	Leu	Glu	Gly	Gln	Arg	Lys	Arg	Arg	Asn	Thr	Ile	His

290		295		300
Glu Phe Lys Lys Ser Ala Lys Thr Thr Leu Ile Lys Ile Asp Pro Ala				
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Leu Lys Ile Lys Thr Lys Lys Val Asn Thr Ala Asp Gln Cys Ala Asn				
		325		330 335
Arg Cys Thr Arg Asn Lys Gly Leu Pro Phe Thr Cys Lys Ala Phe Val				
		340		345 350
Phe Asp Lys Ala Arg Lys Gln Cys Leu Trp Phe Pro Phe Asn Ser Met				
		355		360 365
Ser Ser Gly Val Lys Lys Glu Phe Gly His Glu Phe Asp Leu Tyr Glu				
		370		375 380
Asn Lys Asp Tyr Ile Arg Asn Cys Ile Ile Gly Lys Gly Arg Ser Tyr				
385		390		395 400
Lys Gly Thr Val Ser Ile Thr Lys Ser Gly Ile Lys Cys Gln Pro Trp				
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Ser Ser Met Ile Pro His Glu His Ser Tyr Arg Gly Lys Asp Leu Gln				
		420		425 430
Glu Asn Tyr Cys Arg Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys				
		435		440 445
Phe Thr Ser Asn Pro Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln				
		450		455 460
Cys Ser Glu Val Glu Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly				
465		470		475 480
Leu Met Asp His Thr Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His				
		485		490 495
Gln Thr Pro His Arg His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys				
		500		505 510
Gly Phe Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro				
		515		520 525
Trp Cys Tyr Thr Leu Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile				
		530		535 540
Lys Thr Cys Ala Asp Lys Ala Asp Asp Asp Asp Lys His His His His				
545		550		555 560
His His His				

<210> 5  
 <211> 36  
 <212> DNA

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B

<213> Artificial Sequence

<220>

<223> Oligonucleotide primer targeted to human MSP cDNA

<400> 5

cgcgcggaat tccaccatgg ggtggctccc actcct

36

<210> 6

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide primer targeted to human MSP cDNA

<400> 6

cgcgcgctcg aggcggggct gtgcctcgga cccgca

36

<210> 7

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide primer targeted to human HGF cDNA

<400> 7

cgcgcgctcta gagggacaaa ggaaaagaag aaatac

36

<210> 8

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide primer targeted to human HGF cDNA

<400> 8

cgcgcggaagc tttgtcagcg catgttttaa ttgcac

36

<210> 9

<211> 50

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide primer used to synthesize the Metron Factor-1 linker sequence

<400> 9

tcgagggcgg tggcggttct ggtggcggtg gctccggcgg tggcggttct

50

<210> 10  
 <211> 50  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <223> Oligonucleotide primer used to synthesize the Metron Factor-1 linker sequence  
  
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 <210> 11  
 <211> 50  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <223> Oligonucleotide primer used to insert the tag sequence in Metron Factor-1  
  
 <400> 11  
 agctgacgac gacgacaaac accaccacca ccaccaccac tagggtcgac 50  
  
 <210> 12  
 <211> 50  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <223> Oligonucleotide primer used to insert the tag sequence in Metron Factor-1  
  
 <400> 12  
 agctgtcgac cctagtgggtg gtgggtgggtg tgggtgtttgt cgtcgtcgtc 50  
  
 <210> 13  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <223> Oligonucleotide primer targeted to human HGF cDNA  
  
 <400> 13  
 cgcgcgggat ccgccagccg ctccagcagc accatg 36  
  
 <210> 14  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

47

B



<220>

<223> Oligonucleotide primer targeted to human HGF cDNA

<400> 14

cgcgcggaagc ttgtcagcg catgttttaa ttgcac

36

<210> 15

<211> 52

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide primer used to synthesize the Magic Factor-1 linker sequence

<400> 15

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52

<210> 16

<211> 52

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide primer used to synthesize the Magic Factor-1 linker sequence

<400> 16

ctagagaacc gccaccgccg gagccaccgc caccagaacc gccaccgccc ga

52

<210> 17

<211> 2172

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(2172)

<223>

<400> 17

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Met Trp Val Thr Lys Leu Leu Pro Ala Leu Leu Leu Gln His Val Leu  
1 5 10 15

48

ctg cat ctc ctc ctg ctc ccc atc gcc atc ccc tat gca gag gga caa  
Leu His Leu Leu Leu Leu Pro Ile Ala Ile Pro Tyr Ala Glu Gly Gln  
20 25 30

96

agg aaa aga aga aat aca att cat gaa ttc aaa aaa tca gca aag act  
Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser Ala Lys Thr  
35 40 45

144

48

6

acc cta atc aaa ata gat cca gca ctg aag ata aaa acc aaa aaa gtg	192
Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr Lys Lys Val	
50 55 60	
aat act gca gac caa tgt gct aat aga tgt act agg aat aaa gga ctt	240
Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys Gly Leu	
65 70 75 80	
cca ttc act tgc aag gct ttt gtt ttt gat aaa gca aga aaa caa tgc	288
Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys Gln Cys	
85 90 95	
ctc tgg ttc ccc ttc aat agc atg tca agt gga gtg aaa aaa gaa ttt	336
Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys Glu Phe	
100 105 110	
ggc cat gaa ttt gac ctc tat gaa aac aaa gac tac att aga aac tgc	384
Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg Asn Cys	
115 120 125	
atc att ggt aaa gga cgc agc tac aag gga aca gta tct atc act aag	432
Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile Thr Lys	
130 135 140	
agt ggc atc aaa tgt cag ccc tgg agt tcc atg ata cca cac gaa cac	480
Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His Glu His	
145 150 155 160	
agc tat cgg ggt aaa gac cta cag gaa aac tac tgt cga aat cct cga	528
Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn Tyr Cys Arg Asn Pro Arg	
165 170 175	
ggg gaa gaa ggg gga ccc tgg tgt ttc aca agc aat cca gag gta cgc	576
Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr Ser Asn Pro Glu Val Arg	
180 185 190	
tac gaa gtc tgt gac att cct cag tgt tca gaa gtt gaa tgc atg acc	624
Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser Glu Val Glu Cys Met Thr	
195 200 205	
tgc aat ggg gag agt tat cga ggt ctc atg gat cat aca gaa tca ggc	672
Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met Asp His Thr Glu Ser Gly	
210 215 220	
aag att tgt cag cgc tgg gat cat cag aca cca cac cgg cac aaa ttc	720
Lys Ile Cys Gln Arg Trp Asp His Gln Thr Pro His Arg His Lys Phe	
225 230 235 240	
ttg cct gaa aga tat ccc gac aag ggc ttt gat gat aat tat tgc cgc	768
Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe Asp Asp Asn Tyr Cys Arg	
245 250 255	
aat ccc gat ggc cag ccg agg cca tgg tgc tat act ctt gac cct cac	816
Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys Tyr Thr Leu Asp Pro His	
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acc cgc tgg gag tac tgt gca att aaa aca tgc gct gac aat act atg	864

49

B

Thr	Arg	Trp	Glu	Tyr	Cys	Ala	Ile	Lys	Thr	Cys	Ala	Asp	Asn	Thr	Met	
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Asn	Asp	Thr	Asp	Val	Pro	Leu	Glu	Thr	Thr	Glu	Cys	Ile	Gln	Gly	Gln	
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gga	gaa	ggc	tac	agg	ggc	act	gtc	aat	acc	att	tgg	aat	gga	att	cca	960
Gly	Glu	Gly	Tyr	Arg	Gly	Thr	Val	Asn	Thr	Ile	Trp	Asn	Gly	Ile	Pro	
305					310					315					320	
tgt	cag	cgt	tgg	gat	tct	cag	tat	cct	cac	gag	cat	gac	atg	act	cct	1008
Cys	Gln	Arg	Trp	Asp	Ser	Gln	Tyr	Pro	His	Glu	His	Asp	Met	Thr	Pro	
				325					330					335		
gaa	aat	ttc	aag	tgc	aag	gac	cta	cga	gaa	aat	tac	tgc	cga	aat	cca	1056
Glu	Asn	Phe	Lys	Cys	Lys	Asp	Leu	Arg	Glu	Asn	Tyr	Cys	Arg	Asn	Pro	
			340					345					350			
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Ser	Cys	Ala	Lys	Thr	Lys	Gln	Leu	Arg	Val	Val	Asn	Gly	Ile	Pro	Thr	
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Gln	Cys	Phe	Pro	Ser	Arg	Asp	Leu	Lys	Asp	Tyr	Glu	Ala	Trp	Leu	Gly			
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Met	Lys	Leu	Ala	Arg	Pro	Ala	Val	Leu	Asp	Asp	Phe	Val	Ser	Thr	Ile			
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His	Arg	Gly	Lys	Val	Thr	Leu	Asn	Glu	Ser	Glu	Ile	Cys	Ala	Gly	Ala			
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Ala	Tyr	Tyr	Ala	Lys	Trp	Ile	His	Lys	Ile	Ile	Leu	Thr	Tyr	Lys	Val			
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<400> 18

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Arg	Lys	Arg	Arg	Asn	Thr	Ile	His	Glu	Phe	Lys	Lys	Ser	Ala	Lys	Thr
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Thr	Leu	Ile	Lys	Ile	Asp	Pro	Ala	Leu	Lys	Ile	Lys	Thr	Lys	Lys	Val
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Pro	Phe	Thr	Cys	Lys	Ala	Phe	Val	Phe	Asp	Lys	Ala	Arg	Lys	Gln	Cys
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Leu	Trp	Phe	Pro	Phe	Asn	Ser	Met	Ser	Ser	Gly	Val	Lys	Lys	Glu	Phe
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Gly	His	Glu	Phe	Asp	Leu	Tyr	Glu	Asn	Lys	Asp	Tyr	Ile	Arg	Asn	Cys
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Ile	Ile	Gly	Lys	Gly	Arg	Ser	Tyr	Lys	Gly	Thr	Val	Ser	Ile	Thr	Lys
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Ser	Gly	Ile	Lys	Cys	Gln	Pro	Trp	Ser	Ser	Met	Ile	Pro	His	Glu	His
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Ser	Tyr	Arg	Gly	Lys	Asp	Leu	Gln	Glu	Asn	Tyr	Cys	Arg	Asn	Pro	Arg
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Gly	Glu	Glu	Gly	Gly	Pro	Trp	Cys	Phe	Thr	Ser	Asn	Pro	Glu	Val	Arg
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Tyr	Glu	Val	Cys	Asp	Ile	Pro	Gln	Cys	Ser	Glu	Val	Glu	Cys	Met	Thr
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Cys	Asn	Gly	Glu	Ser	Tyr	Arg	Gly	Leu	Met	Asp	His	Thr	Glu	Ser	Gly
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225					230					235					240
Leu	Pro	Glu	Arg	Tyr	Pro	Asp	Lys	Gly	Phe	Asp	Asp	Asn	Tyr	Cys	Arg
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			260					265					270				
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	450					455					460						
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465					470					475					480		
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			500					505					510				
Ile	Cys	Gly	Gly	Ser	Leu	Ile	Lys	Glu	Ser	Trp	Val	Leu	Thr	Ala	Arg		
		515					520					525					
Gln	Cys	Phe	Pro	Ser	Arg	Asp	Leu	Lys	Asp	Tyr	Glu	Ala	Trp	Leu	Gly		
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Ile	His	Asp	Val	His	Gly	Arg	Gly	Asp	Glu	Lys	Cys	Lys	Gln	Val	Leu		
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Asn Val Ser Gln Leu Val Tyr Gly Pro Glu Gly Ser Asp Leu Val Leu  
565 570 575

Met Lys Leu Ala Arg Pro Ala Val Leu Asp Asp Phe Val Ser Thr Ile  
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Asp Leu Pro Asn Tyr Gly Cys Thr Ile Pro Glu Lys Thr Ser Cys Ser  
595 600 605

Val Tyr Gly Trp Gly Tyr Thr Gly Leu Ile Asn Tyr Asp Gly Leu Leu  
610 615 620

Arg Val Ala His Leu Tyr Ile Met Gly Asn Glu Lys Cys Ser Gln His  
625 630 635 640

His Arg Gly Lys Val Thr Leu Asn Glu Ser Glu Ile Cys Ala Gly Ala  
645 650 655

Glu Lys Ile Gly Ser Gly Pro Cys Glu Gly Asp Tyr Gly Gly Pro Leu  
660 665 670

Val Cys Glu Gln His Lys Met Arg Met Val Leu Gly Val Ile Val Pro  
675 680 685

Gly Arg Gly Cys Ala Ile Pro Asn Arg Pro Gly Ile Phe Val Arg Val  
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Pro Gln Ser

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cct ggg cag cgc tcg cca ttg aat gac ttc caa gtg ctc cgg ggc aca 96  
Pro Gly Gln Arg Ser Pro Leu Asn Asp Phe Gln Val Leu Arg Gly Thr  
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gag cta cag cac ctg cta cat gcg gtg gtg ccc ggg cct tgg cag gag 144  
Glu Leu Gln His Leu Leu His Ala Val Val Pro Gly Pro Trp Gln Glu  
35 40 45

54

B

gat	gtg	gca	gat	gct	gaa	gag	tgt	gct	ggc	cgc	tgt	ggg	ccc	tta	atg	192
Asp	Val	Ala	Asp	Ala	Glu	Glu	Cys	Ala	Gly	Arg	Cys	Gly	Pro	Leu	Met	
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ctg	cca	tgg	act	caa	cac	tgc	ccc	cac	acg	agg	ctg	cgg	cgt	tct	ggg	288
Leu	Pro	Trp	Thr	Gln	His	Ser	Pro	His	Thr	Arg	Leu	Arg	Arg	Ser	Gly	
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cgc	tgt	gac	ctc	ttc	cag	aag	aaa	gac	tac	gta	cgg	acc	tgc	atc	atg	336
Arg	Cys	Asp	Leu	Phe	Gln	Lys	Lys	Asp	Tyr	Val	Arg	Thr	Cys	Ile	Met	
			100					105					110			
aac	aat	ggg	gtt	ggg	tac	cgg	ggc	acc	atg	gcc	acg	acc	gtg	ggc	ggc	384
Asn	Asn	Gly	Val	Gly	Tyr	Arg	Gly	Thr	Met	Ala	Thr	Thr	Val	Gly	Gly	
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Leu	Pro	Cys	Gln	Ala	Trp	Ser	His	Lys	Phe	Pro	Asn	Asp	His	Lys	Tyr	
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Asp	Gly	Asp	Pro	Gly	Gly	Pro	Trp	Cys	Tyr	Thr	Thr	Asp	Pro	Ala	Val	
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cgc	ttc	cag	agc	tgc	ggc	atc	aaa	tcc	tgc	cgg	gag	gcc	gcg	tgt	gtc	576
Arg	Phe	Gln	Ser	Cys	Gly	Ile	Lys	Ser	Cys	Arg	Glu	Ala	Ala	Cys	Val	
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Trp	Cys	Asn	Gly	Glu	Glu	Tyr	Arg	Gly	Ala	Val	Asp	Arg	Thr	Glu	Ser	
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Gly	Arg	Glu	Cys	Gln	Arg	Trp	Asp	Leu	Gln	His	Pro	His	Gln	His	Pro	
	210					215					220					
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55

B



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	290					295					300					
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Gln	Arg	Trp	Asp	Ala	Gln	Ile	Pro	His	Gln	His	Arg	Phe	Thr	Pro	Glu	
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Lys	Tyr	Ala	Cys	Lys	Asp	Leu	Arg	Glu	Asn	Phe	Cys	Arg	Asn	Pro	Asp	
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Gly	Ser	Glu	Ala	Pro	Trp	Cys	Phe	Thr	Leu	Arg	Pro	Gly	Met	Arg	Ala	
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Ala	Phe	Cys	Tyr	Gln	Ile	Arg	Arg	Cys	Thr	Asp	Asp	Val	Arg	Pro	Gln	
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Lys	Pro	Gln	Phe	Thr	Phe	Thr	Ser	Glu	Pro	His	Ala	Gln	Leu	Glu	Glu	
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Asn	Phe	Cys	Arg	Asn	Pro	Asp	Gly	Asp	Ser	His	Gly	Pro	Trp	Cys	Tyr	
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Thr	Met	Asp	Pro	Arg	Thr	Pro	Phe	Asp	Tyr	Cys	Ala	Leu	Arg	Arg	Cys	
		435					440					445				
gct	gat	gac	cag	ccg	cca	tca	atc	ctg	gac	ccc	cca	gac	cag	gtg	cag	1392
Ala	Asp	Asp	Gln	Pro	Pro	Ser	Ile	Leu	Asp	Pro	Pro	Asp	Gln	Val	Gln	
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Phe	Glu	Lys	Cys	Gly	Lys	Arg	Val	Asp	Arg	Leu	Asp	Gln	Arg	Arg	Ser	
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aag	ctg	cgc	gtg	gtt	ggg	ggc	cat	ccg	ggc	aac	tca	ccc	tgg	aca	gtc	1488
Lys	Leu	Arg	Val	Val	Gly	Gly	His	Pro	Gly	Asn	Ser	Pro	Trp	Thr	Val	
				485					490					495		
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56

B

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aag	gag	cag	tgg	ata	ctg	act	gcc	cgg	cag	tgc	ttc	tcc	tcc	tgc	cat	1584
Lys	Glu	Gln	Trp	Ile	Leu	Thr	Ala	Arg	Gln	Cys	Phe	Ser	Ser	Cys	His	
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Met	Pro	Leu	Thr	Gly	Tyr	Glu	Val	Trp	Leu	Gly	Thr	Leu	Phe	Gln	Asn	
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Pro	Gln	His	Gly	Glu	Pro	Ser	Leu	Gln	Arg	Val	Pro	Val	Ala	Lys	Met	
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Ser	Val	Thr	Leu	Asn	Gln	Arg	Val	Ala	Leu	Ile	Cys	Leu	Pro	Pro	Glu	
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Trp	Tyr	Val	Val	Pro	Pro	Gly	Thr	Lys	Cys	Glu	Ile	Ala	Gly	Trp	Gly	
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Glu	Thr	Lys	Gly	Thr	Gly	Asn	Asp	Thr	Val	Leu	Asn	Val	Ala	Phe	Leu	
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aat	gtt	atc	tcc	aac	cag	gag	tgt	aac	atc	aag	cac	cga	gga	cgt	gtg	1920
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Arg	Glu	Ser	Glu	Met	Cys	Thr	Glu	Gly	Leu	Leu	Ala	Pro	Val	Gly	Ala	
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tgt	gag	ggc	gac	tac	ggg	ggc	cca	ctt	gcc	tgc	ttt	acc	cac	aac	tgc	2016
Cys	Glu	Gly	Asp	Tyr	Gly	Gly	Pro	Leu	Ala	Cys	Phe	Thr	His	Asn	Cys	
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Trp	Val	Leu	Glu	Gly	Ile	Ile	Ile	Pro	Asn	Arg	Val	Cys	Ala	Arg	Ser	
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	690					695					700					
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 <213> Homo sapiens

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Arg	Cys	Asp	Leu	Phe	Gln	Lys	Lys	Asp	Tyr	Val	Arg	Thr	Cys	Ile	Met
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Asp	Gly	Asp	Pro	Gly	Gly	Pro	Trp	Cys	Tyr	Thr	Thr	Asp	Pro	Ala	Val
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Trp	Cys	Asn	Gly	Glu	Glu	Tyr	Arg	Gly	Ala	Val	Asp	Arg	Thr	Glu	Ser
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Arg	Asn	Pro	Asp	Gly	Ser	Glu	Arg	Pro	Trp	Cys	Tyr	Thr	Thr	Asp	Pro
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17B

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Glu	Gly	Tyr	Arg	Gly	Thr	Ala	Asn	Thr	Thr	Thr	Ala	Gly	Val	Pro	Cys			
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Lys	Tyr	Ala	Cys	Lys	Asp	Leu	Arg	Glu	Asn	Phe	Cys	Arg	Asn	Pro	Asp			
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Lys	Pro	Gln	Phe	Thr	Phe	Thr	Ser	Glu	Pro	His	Ala	Gln	Leu	Glu	Glu			
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Ala	Asp	Asp	Gln	Pro	Pro	Ser	Ile	Leu	Asp	Pro	Pro	Asp	Gln	Val	Gln			
	450					455					460							
Phe	Glu	Lys	Cys	Gly	Lys	Arg	Val	Asp	Arg	Leu	Asp	Gln	Arg	Arg	Ser			
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Ser	Leu	Arg	Asn	Arg	Gln	Gly	Gln	His	Phe	Cys	Gly	Gly	Ser	Leu	Val			
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Lys	Glu	Gln	Trp	Ile	Leu	Thr	Ala	Arg	Gln	Cys	Phe	Ser	Ser	Cys	His			
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Pro	Gln	His	Gly	Glu	Pro	Ser	Leu	Gln	Arg	Val	Pro	Val	Ala	Lys	Met			
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Val	Cys	Gly	Pro	Ser	Gly	Ser	Gln	Leu	Val	Leu	Leu	Lys	Leu	Glu	Arg			
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59

B

Ser Val Thr Leu Asn Gln Arg Val Ala Leu Ile Cys Leu Pro Pro Glu  
580 585 590

Trp Tyr Val Val Pro Pro Gly Thr Lys Cys Glu Ile Ala Gly Trp Gly  
595 600 605

Glu Thr Lys Gly Thr Gly Asn Asp Thr Val Leu Asn Val Ala Phe Leu  
610 615 620

Asn Val Ile Ser Asn Gln Glu Cys Asn Ile Lys His Arg Gly Arg Val  
625 630 635 640

Arg Glu Ser Glu Met Cys Thr Glu Gly Leu Leu Ala Pro Val Gly Ala  
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Cys Glu Gly Asp Tyr Gly Gly Pro Leu Ala Cys Phe Thr His Asn Cys  
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Trp Val Leu Glu Gly Ile Ile Ile Pro Asn Arg Val Cys Ala Arg Ser  
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His Lys Val Met Arg Leu Gly  
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60

B

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B